



Docket No. 13761-7064

**Certificate of Mailing/Transmission (37 C.F.R. § 1.8(a))**

X Pursuant to 37 C.F.R. § 1.8, I hereby certify that this paper and all enclosures are being deposited with the United States Postal Service as first class mail on the date indicated below in an envelope addressed to the Assistant Commissioner for Patents, Washington D.C. 20231.

Pursuant to 37 C.F.R. § 1.6(d), I hereby certify that this paper and all enclosures are being sent via facsimile on the date indicated below to the attention of Examiner: \_\_\_\_\_ at Facsimile No. \_\_\_\_\_ at \_\_\_\_\_ a.m./p.m.

Dated: June 26, 2002

Name of Person Certifying: \_\_\_\_\_

Printed Name: Bernice E. Worley

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Zandi, et al.

Assignee: University of Southern California

Filing Date: February 19, 2002

Examiner: Not assigned

Serial No.: 10/079,949

Group Art Unit: 1645

Title: Composition and Method for Reconstituting IKB Kinase in Yeast and Methods of Using Same

Assistant Commissioner for Patents  
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In accordance with 37 C.F.R. § 1.56, the references listed on the attached Form PTO-1449 are being brought to the attention of the Examiner for consideration in connection with the examination of the above-identified patent application.

**I. Timing of the Information Disclosure Statement:**

This Information Disclosure Statement is filed:

- ☐ With the new patent application submitted herewith (37 C.F.R. § 1.97(a)).
- ☐ Within three months after the filing date of the application or within three months after the date of entry of the national stage of a PCT application as set forth in 37 C.F.R. § 1.491.
- ☐ Before the mailing of a first Office Action after the filing of a request for continued examination under 37 C.F.R. § 1.114.
- ☒ Before the mailing of a first Office action on the merits. In the event, however, that an Office Action has crossed in the mail with this Information Disclosure Statement:
  - ☒ the Commissioner is hereby authorized to charge Deposit Account No. 50-1192, Docket No. 13761-7064 for the fee (\$180) set forth in 37 C.F.R. § 1.17(p) and any additional required fees.
  - ☐ a statement as specified in 37 C.F.R. § 1.97(e) is provided below.

This Information Disclosure Statement is filed:

- ☐ After the first Office Action and more than three months after the application's filing date; or PCT national stage date of entry filing, or after the mailing of a first Office Action after the filing of a request for continued examination, but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and
- ☐ the Commissioner is hereby authorized to charge Deposit Account No. [ ] for the fee (\$180) set forth in 37 C.F.R. § 1.17(p) and any additional required fees.
- ☐ a statement as specified in 37 C.F.R. § 1.97(e) is provided below.

This Information Disclosure Statement is filed:

- ☐ After the mailing date of either a final rejection or a notice of allowance, whichever occurred first, but on or before the payment of an issue fee, and is accompanied by the fee (\$180.00) set forth in 37 C.F.R. § 1.17(i)(1) and a certification as specified in 37 C.F.R. § 1.97(e), as checked below. This document is to be considered as a petition requesting consideration of the Information Disclosure Statement.

Pursuant to 37 C.F.R. § 1.97(e), the undersigned certifies that:

- ☐ Each item of information contained in the Information Disclosure Statement was first cited in any communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.
- ☐ No item of information contained in this information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

## II. Copies of the Cited Items:

- ☒ Copies of all of the items listed on the attached Form PTO-1449 are enclosed.
- ☐ Copies of only the following items listed on the attached Form PTO-1449 are enclosed: \_\_\_\_\_.
- ☐ Copies of those items which are marked with an asterisk (\*) in the attached Form PTO-1499 are not supplied because they were previously cited by or submitted to the Patent Office in a prior Application No. \_\_\_\_\_, filed \_\_\_\_\_ and relied upon in this application for an earlier filing date under 35 U.S.C. § 120. See 37 C.F.R. § 1.98(d).

- ☐ Copies of those items which are marked with an asterisk (\*\*) in the attached Form PTO-1499 were cited in a foreign examination report in a related case. A copy of the search report and the cited references not already of record in this application are attached hereto.

### III. Concise Explanation of Relevance:

- ☒ A concise explanation of relevance of the items listed on Form PTO-1449 is not given.
- ☐ A concise explanation of relevance of [some of] the items listed on Form PTO-1449 is in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references (copy attached).

### IV. Conclusion:

Citation of the above documents shall not be construed as:

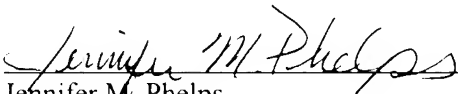
1. an admission that the documents are necessarily prior art with respect to the instant invention;
2. a representation that a search has been made, other than as described above; or
3. an admission that the information cited herein is, or is considered to be, material to patentability as defined in § 1.56(b).

It is respectfully requested that the Examiner indicate consideration of the cited references by returning a copy of the attached form PTO 1449 with initials or other appropriate marks.

The Commissioner is hereby authorized to charge Deposit Account No. 50-1192 and reference Docket No.: 13761-7064 for any additional fees required in connection with the filing of this Information Disclosure Statement.

DATE: June 26, 2002

Respectfully submitted,

By:   
Jennifer M. Phelps  
Registration No.: 48.656

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ATTY. DOCKET NO.

SERIAL NO.

**LIST OF PATENTS AND PUBLICATIONS FOR  
APPLICANT(S)' INFORMATION DISCLOSURE  
STATEMENT**

(Use several sheets if necessary)

TITLE

**COMPOSITION AND METHOD FOR  
RECONSTITUTING I $\kappa$ B KINASE IN YEAST AND  
METHODS OF USING SAME**

13761-7064

10/079,949

INVENTOR

Zandi, et al.

FILING DATE

February 19, 2002

GROUP ART UNIT

1645

## REFERENCE DESIGNATION

## U.S. PATENT DOCUMENTS

EXAMER INITIAL		DOCUMENT NUMBER	DATE	NAME	Class	Subclass	Filing Date If Appropriate
	A1.						
	A2.						
	A3.						
	A4.						

## FOREIGN PATENT DOCUMENTS

EXAMER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	Subclass	TRANSLAT'N	
							yes	no
	B							
	B3							
	B2							
	B4							

## OTHER ART (Include Author, Title, Date, Pertinent Pages, etc.)

C1.	Auphan, N., J. A. DiDonato, C. Rosette, A. Helmberg, and M. Karin 1995. Immunosuppression by glucocorticoids: inhibition of NF-kappa B activity through induction of I kappa B synthesis. Science. 270:286-290.
C2.	Baeuerle, P. A., and D. Baltimore 1988. I kappa B: a specific inhibitor of the NF-kappa B transcription factor. Science. 242:540-546.
C3.	Baud, V., Z.-G. Liu, B. Bennett, N. Suzuki, Y. Xia, and M. Karin 1999. Signaling by proinflammatory cytokines: oligomerization of TRAF2 and TRAF6 is sufficient for JNK and IKK activation and target gene induction via an amino-terminal effector domain. Genes & Develop. 13:1297-1308.
C4.	Beg, A. A., and D. Baltimore 1996. An essential role for NF-kappa-B in preventing TNF-alpha-induced cell death. Science. 274:782-784.
C5.	Beg, A. A., W. C. Sha, R. T. Bronson, S. Ghosh, and D. Baltimore 1995. Embryonic lethality and liver degeneration in mice lacking the RelA component of NF-kB. Nature. 376:167-169.
C6.	Brach, M. A., R. Hass, M. L. Sherman, H. Gunji, and R. Weichselbaum 1991. Ionizing radiation induces expression and binding activity of the nuclear factor kappa B. J. Clin. Invest.. 88:691-695.
C7.	Christianson, T. W., R. S. Sikorski, M. Dante, J. H. Shero, and P. Hieter 1992. Multifunctional yeast high-copy-number shuttle vectors. Gene. 110:119-122.

EXAMINER

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C8.	DiDonato, J. A., M. Hayakawa, D. M. Rothwarf, E. Zandi, and M. Karin 1997. A cytokine-responsive I $\kappa$ B kinase that activates the transcription factor NF- $\kappa$ B. <i>Nature</i> . 388:548-554.
C9.	Gill, J. S., and A. J. Windebank 2000. Ceramide initiates NF $\kappa$ B-mediated caspase activation in neuronal apoptosis. <i>Neurobiol. Dis.</i> 7:448-461.
C10.	Gilmore, T. D., M. Koedood, K. A. Piffat, and D. W. White 1996. Rel/NF- $\kappa$ B proteins and cancer. <i>Oncogene</i> . 13:1367-1378.
C11.	Guttridge, D. C., M. W. Mayo, L. V. Madrid, C. Y. Wang, and A. S. Baldwin, Jr. 2000. NF- $\kappa$ B-induced loss of MyoD messenger RNA: possible role in muscle decay and cachexia. <i>Science</i> . 289:2363-2366.
C12.	Huynh, Q. K., H. Boddupalli, S. A. Rouw, C. M. Koboldt, T. Hall, C. Sommers, S. D. Hauser, J. L. Pierce, R. G. Combs, B. A. Reitz, J. A. Diaz-Collier, R. A. Weinberg, B. L. Hood, B. F. Kilpatrick, and C. T. Tripp 2000. Characterization of the recombinant IKK1/IKK2 heterodimer. <i>J. Biol. Chem.</i> 275:25883-25891.
C13.	Lee, H. H., H. Dadgostar, Q. Cheng, J. Shu, and G. Cheng 1999. NF- $\kappa$ B-mediated up-regulation of Bcl-x and Bfl-1/A1 is required for CD40 survival signaling in B lymphocytes. <i>Proc. Natl. Acad. Sci. U.S.A.</i> 96:9136-9141.
C14.	Lee, J. I., and G. J. Burckart 1998. Nuclear factor kappa B: important transcription factor and therapeutic target. <i>J. Clin. Pharm.</i> 38:981-993.
C15.	Li, N., and M. Karin 1998. Ionizing radiation and short wavelength UV activate NF- $\kappa$ B through two distinct mechanisms. <i>Proc. Natl Acad. Sci U.S.A.</i> 95:13012-13017.
C16.	Li, Q., D. VanAntwerp, D. Mercurio, K. F. Lee, and I. M. Verma 1999. Severe liver degeneration in mice lacking the I $\kappa$ B kinase 2 gene. <i>Science</i> . 284:321-325.
C17.	Liu, Z. G., H. L. Hsu, D. V. Goeddel, and M. Karin 1996. Dissection of TNF receptor 1 effector functions -- JNK activation is not linked to apoptosis while NF- $\kappa$ B activation prevents cell death. <i>Cell</i> . 87:565-576.
C18.	Makris, C., V. L. Godfrey, G. Krahn-Senftleben, T. Takahashi, J. L. Roberts, T. Schwarz, L. Feng, R. S. Johnson, and M. Karin 2000. Female mice heterozygous for IKK gamma/NEMO deficiencies develop a dermatopathy similar to the human X-linked disorder incontinentia pigmenti. <i>Mol. Cell</i> . 5:969-979.
C19.	May, M. J., F. D'Acquisto, L. A. Madge, J. Glockner, J. S. Pober, and S. Ghosh 2000. Selective inhibition of NF- $\kappa$ B activation by a peptide that blocks the interaction of NEMO with the I $\kappa$ B kinase complex. <i>Science</i> . 289:1550-1554.

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C20.	Mercurio, F., H. Zhu, B. W. Murray, A. Shevchenko, B. L. Bennett, J. Li, D. B. Young, M. Barbosa, M. Mann, A. Manning, and A. Rao 1997. IKK-1 and IKK-2: cytokine-activated I $\kappa$ B kinases essential for NF-kappaB activation. Science. 278:860-866.
C21.	Mosialos, G. 1997. The role of Rel/NF-kappa B proteins in viral oncogenesis and the regulation of viral transcription. Sem. Cancer Biol. 8:121-129.
C22.	Mumberg, D., R. Muller, and M. Funk 1994. Regulatable promoters of <i>Saccharomyces cerevisiae</i> : comparison of transcriptional activity and their use for heterologous expression. Nuc. Acids Res. 22:5767-5768.
C23.	Osborn, L., S. Kunkel, and G. J. Nabel 1989. Tumor necrosis factor alpha and interleukin 1 stimulate the human immunodeficiency virus enhancer by activation of the nuclear factor kappa B. Proc. Natl. Acad. Sci. U.S.A. 86:2336-2340.
C24.	Pahl, H. L. 1999. Activators and target genes of Rel/NF-kB transcription factors. Oncogene. 18:6853-6866.
C25.	Ray, A., and K. E. Prefontaine 1994. Physical association and functional antagonism between the p65 subunit of transcription factor NF-kappa B and the glucocorticoid receptor. Proc. Natl. Acad. Sci. U.S.A. 91:752-756.
C26.	Roshak, A. K., J. R. Jackson, K. McGough, M. Chabot-Fletcher, E. Mochan, and L. A. Marshall 1996. Manipulation of distinct NF-kB proteins alters interleukin-1-induced human rheumatoid synovial fibroblast prostaglandin E2 formation. J. Biol. Chem. 271:31496-31501.
C27.	Rothwarf, D. M., E. Zandi, G. Natoli, and M. Karin 1998. IKK-gamma is an essential regulatory subunit of the I $\kappa$ B kinase complex. Nature. 395:297-300.
C28.	Rudolph, D., W.-C. Yeh, A. Wakeham, B. Rudolph, D. Nallainathan, J. Potter, A. J. Elia, and T. W. Mak 2000. Severe liver degeneration and lack of NF-kB activation in NEMO/IKK $\gamma$ -deficient mice. Genes & Develop. 14:854-862.
C29.	Sakurada, S., T. Kato, and T. Okamoto 1996. Induction of cytokines and ICAM-1 by proinflammatory cytokines in primary rheumatoid synovial fibroblasts and inhibition by N-acetyl-L-cysteine and aspirin. Int. Immunol. 8:1483-1493.
C30.	Schreck, R., K. Albermann, and P. A. Baeuerle 1992. Nuclear factor kappa B: an oxidative stress-responsive transcription factor of eukaryotic cells (a review). Free Radic. Res. Commun. 17:221-237.
C31.	Sen, R., and D. Baltimore 1986. Inducibility of kappa immunoglobulin enhancer-binding protein NF-kappa B by a posttranslational mechanism. Cell. 47:921-928.

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C32.	Siebenlist, U., G. Franzoso, and K. Brown 1994. Structure, regulation and function of NF-kappa B. Annu. Rev. Cell Biol. 10:405-455.
C33.	Stehlik, C., R. de Martin, I. Kumabashiri, J. A. Schmid, B. R. Binder, and J. Lipp 1998. Nuclear factor (NF)-kB-regulated X-chromosome-linked iap gene expression protects endothelial cells from tumor necrosis factor -induced apoptosis. J. Exp. Med. 188:211-216.
C34.	VanAntwerp, D. J., S. J. Martin, T. Kafri, D. R. Green, and I. M. Verma 1996. Suppression of TNF-alpha-induced apoptosis by NF-kappa-B. Science. 274:787-789.
C35.	VanAntwerp, D. J., S. J. Martin, I. M. Verma, and D. R. Green 1998. Inhibition of TNF-induced apoptosis by NF-kappa B. Trends Cell Biol. 8:107-111.
C36.	Wang, C. Y., M. W. Mayo, and A. S. Baldwin 1996. TNF- and cancer therapy-induced apoptosis-- potentiation by NF-kappa B. Science. 274:784-787.
C37.	Wang, C. Y., M. W. Mayo, R. G. Korneluk, D. V. Goeddel, and A. S. Baldwin, Jr. 1998. NF-kappa B antiapoptosis: induction of TRAF1 and TRAF2 and c-IAP1 and c-IAP2 to suppress caspase-8 activation. Science. 281:1680-1683.
C38.	Weber, C. K., S. Liptay, T. Wirth, G. Adler, and R. M. Schmid 2000. Suppression of NF-kappaB activity by sulfasalazine is mediated by direct inhibition of IkappaB kinases alpha and beta. Gastroenterology. 119:1209-1218.
C39.	Yin, M.-J., Y. Yamamoto, and R. B. Gaynor 1998. The anti-inflammatory agents aspirin and salicylate inhibit the activity of I(kappa)B kinase-beta. Nature. 396:77-80.
C40.	You, M., P.-T. Ku, R. Hrdlickova, and H. R. Bose, Jr. 1997. ch-IAP1, a member of the inhibitor-of-apoptosis protein family, is a mediator of the antiapoptotic activity of the v-Rel oncoprotein. Mol. Cell. Biol. 17:7328-7341.
C41.	Yujiri, T., M. Ware, C. Widmann, R. Oyer, D. Russell, E. Chan, Y. Zaitso, P. Clarke, K. Tyler, Y. Oka, G. R. Fanger, P. Henson, and G. L. Johnson 2000. MEK kinase 1 gene disruption alters cell migration and c-Jun NH <sub>2</sub> -terminal kinase regulation but does not cause a measurable defect in NF- $\kappa$ B activation. Proc. Natl. Acad. Sci. U.S.A. 97:7272-7277.
C42.	Zandi, E., Y. Chen, and M. Karin 1998. Direct phosphorylation of IkappaB by IKKalpha and IKKbeta: discrimination between free and NF-kappaB-bound substrate. Science. 281:1360-1363.
C43.	Zandi, E., and M. Karin 1999. Bridging the gap: composition, regulation, and physiological function of the I $\kappa$ B kinase complex. Mol. Cell. Biol. 19:4547-4551.

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C44.	Zandi, E., D. M. Rothwarf, M. Delhase, M. Hayakawa, and M. Karin 1997. The IkappaB kinase complex (IKK) contains two kinase subunits, IKKalpha and IKKbeta, necessary for IkappaB phosphorylation and NF-kappaB activation. Cell. 91:243-252.
C45.	Zhang, S. Q., A. Kovalenko, G. Cantarella, and D. Wallach 2000. Recruitment of the IKK signalosome to the p55 TNF receptor: RIP and A20 bind to NEMO (IKK $\gamma$ ) upon receptor stimulation. Immunity. 12:301-311.
C46.	Watson, J.D., Hopkins, N.H., Roberts, L.W., Steitz, L.A., and Weiner, A.M. 1987. In Molecular Biology of the Gene, Vol. 1, pp. 550-594. Benjamin/Cummings, Menlo Park, CA.

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